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L1	6274177	3	L1

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L1: Entry 1 of 3 File: USPT Aug 14, 2001

US-PAT-NO: 6274177
DOCUMENT-IDENTIFIER: US 6274177 B1

TITLE: Method of preparing an extract potent in anti-inflammation and anti-platelet aggregation from Zingiber officinale and pharmaceutical compositions containing said extract

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wu; Tian-Shung	Tainan			TW
Kuo; Sheng-Chu	Taichung			TW
Teng; Che-Ming	Taipei			TW
Ko; Feng-Nien	Taipei			TW

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
National Science Council	Taipei			TW	03

APPL-NO: 09/ 648662 [PALM]
DATE FILED: August 26, 2000

INT-CL: [07] A61 K 35/78

US-CL-ISSUED: 424/756; 424/773
US-CL-CURRENT: 424/756; 424/773

FIELD-OF-SEARCH: 424/195.1, 424/773, 424/756

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	5494668	February 1996	Patwardhan	424/195.1
☐	5683698	November 1997	Chavali et al.	424/195.1
☐	5716928	February 1998	Benet et al.	514/11
☐	5804603	September 1998	Chen	513/630
☐	5908628	June 1999	Hou	424/195.1

OTHER PUBLICATIONS

BRS Computer Abstract JPAB JP407258104A Suzuki "Cancer Metastasis Suppressing Agent", Oct. 1995.*
BRS Computer Abstract JPAB JP07205777 Sugimoto et al "Synthesis Promoter for

Neurotrophy Factor", Jan. 1995.*
BRS Computer Abstract JPAB JP406107556 Iwasaki et al "Chinese Analgesic Composed Exclusively of Herb Drug", Oct. 1995.

ART-UNIT: 161

PRIMARY-EXAMINER: Lilling; Herbert J.

ABSTRACT:

A method of preparing an extract from Zingiber officinale, which is potent in anti-inflammation and anti-platelet aggregation, includes the following steps: a) preparing a crude liquid from rhizomes of ginger by extraction with an organic solvent or by distillation with steam; b) introducing the crude liquid to a reverse phase chromatography column, and eluting the column with water, a first eluent and a second eluent having a polarity weaker than that of the first eluent but stronger than that of chloroform, so that a first eluate resulting from elution of the first eluent and a second eluate resulting from elution of the second eluent are obtained; c) removing the first eluent from the first eluate by evaporation, so that a first concentrated eluate is obtained and is able to used as the potent extract; and d) removing the second eluent from the second eluate by evaporation, so that a second concentrated eluate is obtained and is able to used as the potent extract.

37 Claims, 0 Drawing figures

Generate Collection

L1: Entry 1 of 3 File: USPT Aug 14, 2001

US-PAT-NO: 6274177
DOCUMENT-IDENTIFIER: US 6274177 B1

TITLE: Method of preparing an extract potent in anti-inflammation and anti-platelet aggregation from Zingiber officinale and pharmaceutical compositions containing said extract

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wu; Tian-Shung	Tainan			TW
Kuo; Sheng-Chu	Taichung			TW
Teng; Che-Ming	Taipei			TW
Ko; Feng-Nien	Taipei			TW

US-CL-CURRENT: 424/756; 424/773

CLAIMS:

What is claimed is:

1. A method of preparing a product potent in anti-inflammation or in anti-platelet aggregation from rhizomes of Zingiber officinale comprising the following steps:

a) preparing a crude liquid from rhizomes of Zingiber officinale;

b) introducing the crude liquid to a reverse phase chromatography column, and eluting the column with water, a first eluent and a second eluent in sequence, said second eluent having a polarity weaker than that of the first eluent but stronger than that of chloroform, so that a first eluate resulting from elution of the first eluent and a second eluate resulting from elution of the second eluent are obtained;

c) removing the first eluent from the first eluate by evaporation, so that a first concentrated eluate is obtained and is able to be used as the potent product; and

d) removing the second eluent from the second eluate by evaporation, so that a second concentrated eluate is obtained and is able to used as the potent product;

wherein step a) comprises steps i) to iv), or comprises step I), step I'), or step I"), wherein said steps i) to iv) are:

i) shedding fresh rhizomes of Zingiber officinale and filleting the resulting mixture to obtain a filtrate and a residue;

ii) extracting the filtrate with a first organic solvent, recovering the resulting extraction solution of the first organic solvent, and evaporating the first organic solvent from the extraction solution to obtain a first concentrated extraction solution;

iii) extracting the residue with a second organic solvent, recovering the resulting extraction solution of the second organic solvent, and evaporating

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Patent Number Information

Application Number: 09/648662 **Order This File** **Assignments**
Filing Date: **08/26/2000**
Effective Date: **08/26/2000**
Application Received: **08/28/2000**
Patent Number: **6274177**
Issue Date: **08/14/2001**
Date of Abandonment: **00/00/0000**
Attorney Docket Number: **CHEN-0085 (108330.00080)**
Status: **150 / PATENTED CASE**
Confirmation Number: **6956**

Examiner Number: **60670 / LILLING, HERBERT**
Group Art Unit: **1651**
Class/Subclass: **424/756.000**
Lost Case: **NO**
Interference Number:
Unmatched Petition: **NO**
L&R Code: Secrecy Code:**1**
Third Level Review: **NO**
Secrecy Order: **NO**
Status Date: **07/26/2001**

Title of Invention: **METHOD OF PREPARING AN EXTRACT POTENT IN ANTI-INFLAMMATION AND ANTI-PLATELET AGGREGATION FROM ZINGIBER OFFICINALE AND PHARMACEUTICAL COMPOSITIONS CONTAINING SAID EXTRACT**

Bar Code	Location	Location Date	Chrg to Location	Charge to Name	Emp. ID	Infra Loc
09648662	**9200 FILE REPOSITORY (FRANCONIA)**	**06/25/2002**	**No Charge to Location**	**No Charge to Name**	**ABAIG**	

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Attorney Docket # _____ Search

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Appln Info | **Contents** | Petition Info | Atty/Agent Info | Continuity Data | Foreign Data

Date	Status	Code	Description
11/15/2002		FWDX	DATE FORWARDED TO EXAMINER
10/28/2002	71	ELC.	RESPONSE TO ELECTION / RESTRICTION
10/01/2002	41	MCTRS	MAIL RESTRICTION REQUIREMENT
10/01/2002	40	CTRS	REQUIREMENT FOR RESTRICTION / ELEC
01/16/2002	30	DOCK	CASE DOCKETED TO EXAMINER IN GAU
07/19/2001	20	OIPE	APPLICATION DISPATCHED FROM OIPE
07/18/2001		C.AD	CORRESPONDENCE ADDRESS CHANGE
07/03/2001		SCAN	APPLICATION SCANNED
06/22/2001	19	IEXX	INITIAL EXAM TEAM NN

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33. The pharmaceutical composition according to claim 32, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

34. The pharmaceutical composition according to claim 33, wherein said second organic solvent is acetone.

35. The pharmaceutical composition according to claim 27, wherein step a) comprises step I').

36. The pharmaceutical composition according to claim 27, wherein step a) comprises step I").

37. A pharmaceutical composition for the inhibition of aggregation of platelet, which comprises a therapeutically effective amount of the second concentrated eluate prepared in step d) of the method according to any one of claims 1 to 13, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

15. The pharmaceutical composition according to claim 14, wherein step a) comprises steps i) to iv).

16. The pharmaceutical composition according to claim 15, wherein said first organic solvent is ethyl ether.

17. The pharmaceutical composition according to claim 16, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

18. The pharmaceutical composition according to claim 17, wherein said second organic solvent is acetone.

19. The pharmaceutical composition according to claim 14, wherein step a) comprises step I).

20. The pharmaceutical composition according to claim 19, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

21. The pharmaceutical composition according to claim 20, wherein said second organic solvent is acetone.

22. The pharmaceutical composition according to claim 14, wherein step a) comprises step I').

23. The pharmaceutical composition according to claim 14, wherein step a) comprises step I").

24. A pharmaceutical composition for the inhibition of aggregation of platelet, which comprises a therapeutically effective amount of the first concentrated eluate prepared in step c) of the method according to any one of claims 1 to 13, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

25. An anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of the first concentrated eluate prepared in step c) of the method according to any one of claims 1 to 13, as an active ingredient in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

26. An anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of the second concentrated eluate prepared in step d) of the method according to any one of claims 1 to 13, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

27. A pharmaceutical composition for the inhibition of aggregation of platelet, which comprises a therapeutically effective amount of said crude liquid prepared in step a) of the method according to claim 1, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

28. The pharmaceutical composition according to claim 27, wherein step a) comprises steps i) to iv).

29. The pharmaceutical composition according to claim 28, wherein said first organic solvent is ethyl ether.

30. The pharmaceutical composition according to claim 28, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

31. The pharmaceutical composition according to claim 30, wherein said second organic solvent is acetone.

32. The pharmaceutical composition according to claim 27, wherein step a) comprises step I).

the second organic solvent from the extraction solution to obtain a second concentrated extraction solution; and

iv) combining the first concentrated extraction solution and the second concentrated extraction solution to obtain the crude liquid;

said step I) is:

I) extracting powder of dried rhizomes of Zingiber officinale with the second organic solvent, recovering the resulting extraction solution of the second organic solvent, and evaporating the second organic solvent from the extraction solution to obtain the crude liquid;

said step I') is:

I') steam distilling powder of dried rhizomes of Zingiber officinale, and concentrating the resulting distillate by evaporation to obtain the crude liquid; and

said step I") is:

I") extracting powder of dried rhizomes of Zingiber officinale with supercritical CO.sub.2, recovering the resulting extraction solution of the supercritical CO.sub.2, and evaporating CO.sub.2 from the extraction solution to obtain the crude liquid.

2. The method according to claim 1, wherein the product potent in anti-inflammation or in anti-platelet aggregation comprises 0-10 mg 6-shogaol per gram of the product, 1-150 mg 6-gingerol per gram of the product, and 0-40 mg 6-dehydrogingerdione per gram of the product.

3. The method according to claim 1, wherein said first eluent is methanol, and said second eluent is acetone.

4. The method according to claim 3, wherein step a) comprises steps i) to iv).

5. The method according to claim 4, wherein said first organic solvent is ethyl ether.

6. The method according to claim 4, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

7. The method according to claim 6, wherein said second organic solvent is acetone.

8. The method according to claim 3, wherein step a) comprises step I).

9. The method according to claim 8, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

10. The method according to claim 9, wherein said second organic solvent is acetone.

11. The method according to claim 3, wherein step a) comprises step I').

12. The method according to claim 3, wherein step a) comprises step I").

13. The method according to claim 3, wherein said reverse phase chromatography column is packed with a porous resin.

14. An anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of a crude liquid prepared in step a) of the method according to claim 1, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

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Search Results - Record(s) 1 through 3 of 3 returned.

1. 6274177. 26 Aug 00; 14 Aug 01. Method of preparing an extract potent in anti-inflammation and anti-platelet aggregation from Zingiber officinale and pharmaceutical compositions containing said extract. Wu; Tian-Shung, et al. 424/756; 424/773. A61K035/78.

2. US 20020044979 A1. Antifungal composition comprises a product prepared from rhizomes of Zingiber officinale. KO, F, et al. A61K007/06 A61K035/78.

3. US 6274177 B1. Preparing an extract of the Zingiber officinale rhizome, useful as anti-inflammatory or anti- aggregant, comprises eluting the reverse phase chromatography column containing a crude extract with water, a first and second eluent. KO, F, et al. A61K035/78.

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6274177	3

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L1: Entry 1 of 3 File: USPT Aug 14, 2001

US-PAT-NO: 6274177
DOCUMENT-IDENTIFIER: US 6274177 B1

TITLE: Method of preparing an extract potent in anti-inflammation and anti-platelet aggregation from Zingiber officinale and pharmaceutical compositions containing said extract

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wu; Tian-Shung	Tainan			TW
Kuo; Sheng-Chu	Taichung			TW
Teng; Che-Ming	Taipei			TW
Ko; Feng-Nien	Taipei			TW

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
National Science Council	Taipei			TW	03

APPL-NO: 09/ 648662 [PALM]
DATE FILED: August 26, 2000

INT-CL: [07] A61 K 35/78

US-CL-ISSUED: 424/756; 424/773
US-CL-CURRENT: 424/756; 424/773

FIELD-OF-SEARCH: 424/195.1, 424/773, 424/756

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	5494668	February 1996	Patwardhan	424/195.1
☐	5683698	November 1997	Chavali et al.	424/195.1
☐	5716928	February 1998	Benet et al.	514/11
☐	5804603	September 1998	Chen	513/630
☐	5908628	June 1999	Hou	424/195.1

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BRS Computer Abstract JPAB JP407258104A Suzuki "Cancer Metastasis Suppressing Agent", Oct. 1995.*
BRS Computer Abstract JPAB JP07205777 Sugimoto et al "Synthesis Promoter for

Neurotrophy Factor", Jan. 1995.*
BRS Computer Abstract JPAB JP406107556 Iwasaki et al "Chinese Analgesic Composed Exclusively of Herb Drug", Oct. 1995.

ART-UNIT: 161

PRIMARY-EXAMINER: Lilling; Herbert J.

ABSTRACT:

A method of preparing an extract from Zingiber officinale, which is potent in anti-inflammation and anti-platelet aggregation, includes the following steps: a) preparing a crude liquid from rhizomes of ginger by extraction with an organic solvent or by distillation with steam; b) introducing the crude liquid to a reverse phase chromatography column, and eluting the column with water, a first eluent and a second eluent having a polarity weaker than that of the first eluent but stronger than that of chloroform, so that a first eluate resulting from elution of the first eluent and a second eluate resulting from elution of the second eluent are obtained; c) removing the first eluent from the first eluate by evaporation, so that a first concentrated eluate is obtained and is able to used as the potent extract; and d) removing the second eluent from the second eluate by evaporation, so that a second concentrated eluate is obtained and is able to used as the potent extract.

37 Claims, 0 Drawing figures

L1 QUE 6 (W) GINGEROL AND PHARMACEUTICAL

End of Result Set

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L3: Entry 1 of 1 File: DWPI Jan 9, 1990

DERWENT-ACC-NO: 1990-053524
DERWENT-WEEK: 199733

TITLE: Anti-parasite agent - contg. 6-shogaol and/or 6-gingerol

PATENT-ASSIGNEE: TSUMURA & CO (TSUR)

PRIORITY-DATA: 1988JP-0153564 (June 23, 1988)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 02004711 A	January 9, 1990		005	
JP 2629844 B2	July 16, 1997		004	A61K031/12

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
JP 02004711A	June 23, 1988	1988JP-0153564	
JP 2629844B2	June 23, 1988	1988JP-0153564	
JP 2629844B2		JP 2004711	Previous Publ.

INT-CL (IPC): A61K 31/12; C07C 49/25

ABSTRACTED-PUB-NO: JP 02004711A
BASIC-ABSTRACT:

New anti-parasite agent contains (6) - Shogaol and/or (6) - Gingerole as effective components.

USE/ADVANTAGE - Anti-parasite agent for digestive tract.

In an example, the (6) - Shogaol and (6) - Gingerol are made into double dilution series by ethanol, and each of the solns. is added to a physiological sodium chloride soln. so that the rate of each soln. becomes 1% (w/v). The solns. are pipetted into a serum tube (Greiner, Solingen, W-Germany). The final concn. of each component is determined to be 1 mg/ml to 15.625 microg/l. Next, 8-12 Anisakidae larva obtd. by Pepsin-digesting internal organs of walleye pollack are distributed to each tube. These are kept warm at 37 deg.C to judge whether they are killed or not after 24 hrs. As a result, the least effective concn. at which the (6) - Shogaol and (6) - Gingerol cause all polypido motions to disappear is 62.5 microg/ml and 250 microg/ml, respectively. LD50 of (6) Shogaol and (6) - Gingerol is 50.9 mg/kg and 25.0 mg/kg in case of intravenous injection, and 687.0 mg/kg and 250.0 mg/kg in case of oral dosage.

ABSTRACTED-PUB-NO: JP 02004711A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/0

DERWENT-CLASS: B05
CPI-CODES: B10-E02; B12-B04;

United States Patent ***6,264,928***

Jean , et al. **July 24, 2001**

Use of shogaols and gingerols for preparing deodorant compositions

Abstract

A method is provided for suppressing body odors in a human by administering orally to the human or applying to the skin of the human, at least one compound chosen from the group consisting of shogaols and gingerols. The compound corresponds to the general formula: ##STR1## in which X represents: either --CH.dbd.CH--, in which case n is equal to 1, 2, 4, 6, or 8; --CH.sub.2 --CH(OH)--, in which case n is equal to 2, 4, 6 or 8.

Inventors: **Jean; Daniel** (Vic-le-Comte, FR); **Cariel; Leon** (Paris, FR)

Assignee: **Societe d'Etudes et de Recherches en Pharmacognosie** (Paris, FR)

Appl. No.: **341383**

Filed: **September 7, 1999**

PCT Filed: **January 8, 1998**

PCT NO: **PCT/FR98/00025**

371 Date: **September 7, 1999**

102(e) Date: **September 7, 1999**

PCT PUB.NO.: **WO98/30201**

PCT PUB. Date: **July 16, 1998**

Foreign Application Priority Data

Jan 09, 1997[FR] 97 00142

Jan 09, 1997[FR] 97 00143

Current U.S. Class: **424/65**; 424/401

Intern'l Class: A61K 007/32; A61K 007/00

Field of Search: 424/65,76.1,401

References Cited [Referenced By]

Foreign Patent Documents

334967	Oct., 1989	EP.
750908	Jan., 1997	EP.
WO 93/23061	Nov., 1993	WO.

Other References

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Database WPI, Derwent Publications Ltd., XP002044592, Week 9729, Publication No. JP 09 124 677 to Eba Kashohin KK.
Database WPI, Derwent Publications Ltd., XP002044593, Week 8934, Publication No. JP 01 180 817 to Morishita Jintan KK.
STN, Serveur de Bases de Donnees, XP002044589, vol. 101, AN=235404.
Patent Abstracts of Japan, vol. 95, No. 010, Publication No. JP 07 171209 to Matsushita Electric Works.
STN, Serveur de Bases de Donnees, XP002044590, AN=90018412.
STN, Serveur de Bases de Donnees, XP002044591, vol. 106, AN=89987.
Database WPI, Derwent Publications Ltd., XP002066395, Week 9439, Publication No. JP 06 239 736 to Pola Chem Ind. Inc.
Database WPI, Derwent Publications Ltd., XP002066396, Week 9431, Publication No. JP 06 183 959 to Pola Chem Ind. Inc.
Database WPI, Derwent Publications Ltd., XP002066397, Week 8217, Publication No. JP 57 046 914 to Tsumura Juntendo KK.

Primary Examiner: Dodson; Shelley A.
Assistant Examiner: George; Konata M.
Attorney, Agent or Firm: Alston & Bird LLP

Claims

What is claimed is:

1. A method for suppressing body odors in a human comprising administering orally to said human or applying to the skin of said human, at least one compound chosen from the group which consists of shogaols and gingerols.

2. A method according to claim 1, wherein the compound corresponds to the general formula (I):

in which X represents: ##STR4##

either --CH.dbd.CH--, in which case n is equal to 1, 2, 4, 6, or 8;

--CH.sub.2 --CH(OH)--, in which case n is equal to 2, 4, 6 or 8.

3. A method according to claim 1, wherein the compound is used in the form of a crude or purified extract of a plant belonging to the Zingiberacea family, the said extract optionally being combined with one or more other active substances and/or one or more suitably selected excipients.

4. A method according to claim 3, wherein said crude extract contains an amount of compound between 1 and 5% by weight relative to the dry weight of the said extract.

5. A method according to claim 3, wherein the crude extract of the plant belonging to the Zingiberacea family is obtained from fresh or dry rhizomes of the said plant:

by macerating ground material of these rhizomes at a temperature of between 10 and 35.degree. C., followed by one or more extractions of this ground material at reflux, or by subjecting ground material of the said rhizomes to percolation at a temperature of between 10 and 35.degree. C., each of these operations (maceration, extractions at reflux and percolation) being performed using a suitable organic solvent or a mixture of suitable organic solvent and, if desired,

by removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

6. A method according to claim 3, wherein the purified extract contains an amount of compound at least equal to 75% by weight relative to the dry weight of said extract.

7. A method according to claim 5, wherein the purified extract of the plant belonging to the Zingiberacea family is obtained:

by subjecting said crude extract, after optional removal of the solvent(s) it contains and/or its uptake in water, to one or more counter-current extractions using a water-immiscible organic solvent or a mixture of water-immiscible organic solvents and,

removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

8. A method according to claim 3, wherein the plant of the Zingiberacea family is chosen from the group consisting of the species Alpina galanga, Alpinia officinarum, Zingiber officinalis, Zingiber cassumunar and Zingiber zerumbet.

9. A method according to claim 1, wherein said at least one compound is contained in a pharmaceutical composition comprising the compound as active principle, optionally combined with one or more other active principles, and at least one pharmaceutically acceptable excipient.

10. A method according to claim 1, wherein said at least one compound is contained in a cosmetic composition comprising the compound as active substance, optionally combined with one or more other active substances, and at least one suitable selected excipient.

11. A method according to claim 1, wherein said at least one compound is contained in a dietary composition comprising the compound as active substance, optionally combined with one or more other active substances, and at least one suitable selected excipient.

12. A shogaol corresponding to the general formula: ##STR5##

in which X represents --CH.dbd.CH-- and n is equal to 1.

13. A crude extract of a plant belonging to the genus Alpinia, wherein said extract contains an amount of shogaol according to claim 12 of between about 1% and about 5% by weight relative to the dry weight of the said extract.

14. A crude extract according to claim 13, wherein said extract is obtained from fresh or dry rhizomes of the said plant:

by macerating ground material of these rhizomes at a temperature of between 10 and 35.degree. C., followed by one or more extractions of this ground material at reflux, or by subjecting ground material of the said rhizomes to percolation at a temperature of between 10 and 35.degree. C., each of these operations (maceration, extractions at reflux and percolation) being performed using a suitable organic solvent or a mixture of suitable organic solvents and, if desired,

by removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

15. A crude extract according to claim 13, wherein said extract is an extract of Alpinia galanga.

16. A purified extract of a plant belonging to the genus Alpinia, wherein said extract contains an amount of shogaol according to claim 12 at least equal to 75% by weight relative to the dry weight of the said extract.

17. A purified extract according to claim 16, wherein said extract is obtained:

by subjecting a crude extract of a plant belonging to the genus Alpinia, after optional removal of the solvent(s) it contains and/or its uptake in water, to one or more counter-current extractions using a water-immiscible organic solvent or a mixture of water-immiscible organic solvents and, if desired,

by removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

18. A purified extract according to claim 16, wherein said extract is an extract of Alpinia galanga.

19. A deodorant composition comprising a shogaol according to claim 12 as active substance.

20. A deodorant composition according to claim 19, wherein said composition is a pharmaceutical composition which comprises [3]-shogaol as active principle, optionally combined with one or more other active principles and at least one pharmaceutically acceptable excipient.

21. A deodorant composition according to claim 19, wherein said composition is a cosmetic composition which comprises [3]-shogaol as active substance, optionally combined with one or more other active substances, and at least one suitably selected excipient.

22. A deodorant composition according to claim 19, wherein said composition is a dietary composition which comprises [3]-shogaol as active substance, optionally combined with one or more other active substances, and at least one suitable selected excipient.

Description

The present invention relates to the use of shogaols and gingerols for the preparation of deodorant compositions.

The odour of the skin is produced by the secretions of the sweat glands and the sebaceous glands.

The sweat glands produce sweat which consists of water containing a larger or smaller amount of mineral salts and organic substances (lactic acid, urea, etc.), while the sebaceous glands secrete sebum which is mainly formed from fatty substances: cholesterol and its esters, steric acid and palmitic acid and their esters.

Studies [Shelley et al., Arch. Dermatol. Syphilol., 68, 430 (1973)] have shown that the sebaceous and sweat secretions are odourless at the time of production. The odours are produced subsequently by the action of commensal skin bacteria, this action being exerted essentially on apocrine sweat and the sebum on account of their richness in organic substance. Ecrine seat, which is more abundant but has a poorer organic matter content than apocrine sweat, plays only a small part in the creation of odours, although it can play an indirect role by promoting the dispersion of the apocrine sweat components by way of its volume.

Thus, the decomposition of the secretions of the sweat glands and sebaceous glands by the bacterial flora naturally present on the skin, probably in combination with a decomposition of the proteins of the horny layer, gives rise to many highly odorous molecules.

Three types of product which can be used exclusively externally are currently available to counter this phenomenon, which exists over the entire surface of the body but which is particularly pronounced in the pilous regions (armpits, inguinal folds, pubic region, etc.) and palmoplantar regions:

products known as antiperspirants, which are aimed at reducing the production of sweat,

producing which are aimed at limiting the local microbial proliferation and thus the decomposition of the skin secretions, and

products which are aimed at neutralizing, as they are produced, the substances derived from this decomposition which are responsible for the unpleasant odours.

Although, in general, these products show a certain level of efficacy, they have the drawback, on account of their formulation and/or their presentation, of being adapted and, consequently, limited to application to a specific region of the body: armpits, genital region or feet, whereas it would be highly desirable to have available products for universal use, allowing treatment of all the regions of the body which are concerned.

Moreover, certain individuals suffer from veritable perspiration disorders such as ephidrosis, which corresponds to an abnormally high production of sweat, or bromidrosis, which is characterized by the production of particularly fetid sweat, and which are a considerable indisposition for sufferers themselves and for people in their vicinity. For these individuals, the current absence of products capable of systemically treating their complaint is a very real handicap.

Lastly, besides the fact that a body hygiene product needs to be free of toxicity, in particular when it is a deodorant, the suspicion expressed to an every greater extent by many consumers towards products of chemical origin drives them to select by preference products of natural origin.

The problem consequently arises of providing products which are capable of effectively preventing the production of body odours and of doing so both when they are administered systemically and when they are used locally, which can, in the latter case, be applied to any region of the body, which, furthermore, lack toxicity and which also have the advantage of being products of natural origin.

In the context of their studies, the inventors have now found that shogaols and gingerols, compounds which correspond to the general formula (I) below: ##STR2##

in which:

X represents --CH.dbd.CH-- in the case of shogaols, while

X represents --CH.sub.2 --CH(OH)-- in the case of gingerols,

and which are present in plants of the Zingiberacea family, are, unexpectedly, endowed with pronounced deodorant properties, not only when they are applied to the skin but also when they are ingested orally, while at the same time being non-toxic, which makes them advantageous for the preparation of deodorant compositions for the body, which can be used systemically or locally.

A subject of the present invention is thus the use of at least one compound chosen from the group which comprises shogaols and gingerols for the preparation of a deodorant composition.

In accordance with the invention, the compound is preferably chosen from the shogaols corresponding to the general formula (I) mentioned above in which, with X representing --CH.dbd.CH--, n is equal to 1, 2, ,4, 6 or 8, and which are respectively known as [3]-shogaol, [4]-shogaol, [6]-shogaol, [8]-shogaol and [10]-shogaol, and the gingerols which correspond to the general formula (I) mentioned above in which, with X representing --CH.sub.2 --CH(OH)--, n is equal to 2, 4, 6 or 8, and which are known under the respective names [4]-gingerol, [6]-gingerol, [8]-gingerol and [10]-gingerol.

Shogaols and gingerols can be extracted, by any extraction process known per se, from the rhizomes of many Zingiberacea plants and, more particularly, from those belonging to the genera Alpinia and Zingiber. As examples, [3]-shogaol, [6]-shogaol and [8]-shogaol can be extracted from plants of the genus Alpinia, such as Alpinia galanga or Alpinia officinarum, while [4]-shogaol, [10]-shogaol and the gingerols can be extracted from plants of the genus Zingiber, such as Zingiber officinalis, Zingiber cassumunar and Zingiber zerumbet.

Shogaols and gingerols can also be obtained by chemical synthesis, for example according to the processes described by Banno and Mukaiyama, Bull, Chem. Soc. Japan, 49 (5), 1453-1454 (1976).

According to a first preferred embodiment of the invention, the compound is used in the form of a crude or purified extract of a plant belonging to the Zingiberacea family, the said extract optionally being combined with one or more other active substances and/or which one or more suitably selected excipients.

According to one advantageous arrangement of this preferred embodiment, the crude Zingiberacea extract contains an amount of compound of between about 1% and about 5% by weight relative to the dry weight of the said extract.

In accordance with the invention, such a crude extract is obtained from fresh or dry rhizomes of the said

plant:

by macerating ground material of these rhizomes at a temperature of between 10 and 35.degree. C., followed by one or more extractions of this ground materials at reflux, or by subjecting ground material of the said rhizomes to percolation at a temperature of between 10 and 35.degree. C., each of these operations (maceration, extractions at reflux and percolation) being performed using a suitable organic solvent or a mixture of suitable organic solvents and, if desired,

by removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

The maceration of the ground rhizome material, prior to its extraction, mainly has the effect of improving the contact between the plant tissues and the extraction solvent(s). Its duration can be between about twelve hours and one week depending on the state of freshness of the rhizomes used.

For the maceration, extractions at reflux and percolation of the ground material, water-miscible organic solvents are preferably used, the solvents having a relative low boiling point so as to be easy to remove subsequently by simple evaporation, such as ethanol, methanol or acetone, or mixtures thereof with water. However, since shogaols and gingerols are soluble in many organic solvents, it is also possible to use other organic solvents, such as ethyl acetate, ethyl ether, chloroform or methylene chloride.

According to another advantageous arrangement of this preferred embodiment of the invention, the purified Zingiberacea extract contains an amount of compound at least equal to 75% by weight relative to the dry weight of the said extract.

Advantageously, such a purified extract is obtained:

by subjecting a crude extract as defined above, after optional removal of the solvent(s) it contains and/or its uptake in water, to one or more counter-current extractions using a water-immiscible organic solvent or a mixture of water-immiscible organic solvents and, if desired,

by removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

The water-immiscible organic solvent(s) which is (are) useful for carrying out the said counter-current extractions is (are) chosen in particular from ethyl acetate, ethyl ether, chloroform and methylene chloride, and mixtures thereof.

In a particularly preferred manner, whether it is crude or purified, the extract is an extract of a Zingiberacea plant chosen from the group which comprises Alpinia galanga, Alpinia officinarum, Zingiber officinalis, Zingiber cassumunar and Zingiber zerumbet.

According to another preferred embodiment of the invention, the deodorant composition is formulated for oral administration, for example in the form of a powder, a drinkable suspension or solution, a syrup, tablets or gel-capsules.

According to yet another preferred embodiment of the invention, the deodorant composition is formulated for local application, for example in the form of a dermal powder, solution, suspension, gel or cream.

According to yet another embodiment of the invention, the deodorant composition is a pharmaceutical composition which comprises the compound as active principle, optionally combined with one or more

other active principles, and at least one pharmaceutically acceptable excipient. Such a pharmaceutical composition, which can be administered systemically and in particular orally, or locally, finds application in the treatment of dyshidrosis and, more particularly, that of bromidrosis.

As a variant, the deodorant composition is a cosmetic composition which comprises the compound as active substance, optionally combined with one or more other active substances, and at least one suitably selected excipient.

According to yet another variant, the deodorant composition is a dietary composition which comprises the compound as active substance, optionally combined with one or more other active substances, and at least one suitable selected excipient.

Such cosmetic and dietary compositions can advantageously be used as body deodorants to prevent the production of unpleasant odours associated in particular with perspiration.

The invention encompasses, for the abovementioned use, both shogaols known per se, such as [4]-shogaol, [6]-shogaol, [8]-shogaol and [10]-shogaol [Connell and Sutherland, Aust. J. Chem., 22 (5), 1033-1043 (1969)], but whose deodorant properties were neither known nor suggested hitherto, and a new shogaol which is [3]-shogaol, corresponding to formula (II) below: ##STR3##

and which represents, on account of its particularly pronounced deodorant properties, the shogaol preferably used in the invention.

As mentioned above, [3]-shogaol can be obtained in particular from a plant of the genus Alpinia, by means of a process comprising:

the preparation of a crude extract from fresh or dry rhizomes of this plant,

the purification of the crude extract thus obtained, followed by chromatographic separation of this [3]-shogaol from the other shogaols which may be present in the purified extract.

A subject of the invention is also a crude extract of a plant belonging to the genus Alpinia, characterized in that it contains an amount of [3]-shogaol of between about 1% and about 5% by weight relative to the dry weight of the said extract.

In accordance with the invention, this extract is obtained from fresh or dry rhizomes of the said plant:

by macerating ground material of these rhizomes at a temperature of between 10 and 35.degree. C., followed by one or more extractions of this ground material at reflux, or by subjecting ground material of the said rhizomes to percolation at a temperature of between 10 and 35.degree. C., each of these operations (maceration, extractions at reflux and percolation) being performed using a suitable organic solvent or a mixture of suitable organic solvents and, if desired,

by removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

According to a preferred embodiment of the invention, the said crude extract is an extract of Alpinia galanga.

A subject of the invention is also a purified extract of a plant belonging to the genus Alpinia, characterized in that it contains an amount of [3]-shogaol at least equal to 75% by weight relative to the

dry weight of the said extract.

Advantageously, this purified extract is obtained:

by subjecting a crude extract as defined above, after optional removal of the solvent(s) it contains and/or its uptake in water, to one or more counter-current extractions using a water-immiscible organic solvent or a mixture of water-immiscible organic solvents and, if desired,

by removing the solvent(s) from the extract thus obtained in order to obtain a dry extract.

This purified extract is preferably an extract of Alpinia galanga.

Such crude or purified extracts of Alpinia have been themselves found to be endowed with pronounced deodorant properties when they are administered systemically or applied locally, while at the same time being free of toxicity, and are consequently particularly suitable for the preparation of a deodorant composition in accordance with the invention. To this end, they can be used either in their native form as dry powders or aqueous or alcoholic solutions, or in the form of more complex formulations, optionally combined with other active substances.

A subject of the present invention is also a deodorant composition, characterized in that it comprises [3]-shogaol as active substance.

According to a first embodiment, this composition is a pharmaceutical composition which comprises [3]-shogaol as active principle, optionally combined with one or more other active principles and at least one pharmaceutically acceptable excipient.

According to another embodiment, this composition is a cosmetic composition which comprises [3]-shogaol as active substance, optionally combined with one or more other active substances, and at least one suitably selected excipient.

According to yet another embodiment, this composition is a dietary composition which comprises [3]-shogaol as active substance, optionally combined with one or more other active substances, and at least one suitably selected excipient.

In addition to the preceding arrangements, the invention also comprises other arrangements which will emerge from the remainder of the description which follows, which refers to examples for the preparation of extracts of rhizomes from plants of the Zingiberacea family which can be used in accordance with the invention, to an example of the production of [3]-shogaol and examples for the demonstration of the deodorant activities of these extracts and of this [3]-shogaol, and which refers to the attached FIG. 1 which shows the mass spectrum of [3]-shogaol.

It goes without saying, however, that these examples are given purely for the purpose of illustrating the subject of the invention, of which they in no way constitute a limitation.

EXAMPLE 1

PREPARATION OF A CRUDE EXTRACT OF ALPINIA GALANGA RHIZOMES

One kilogram of fresh Alpinia galanga rhizomes is ground coarsely, taking care not to cause excessive heating of the ground parts. The water content of the ground material thus obtained is determined and it

is macerated in 7 litres of ethanol whose titer is chosen such that, taking the water content of the ground material into account, the maceration solvent is 50% ethanol.

After macerating for 24 hours at about 20.degree. C., the ground material is extracted at reflux with the maceration solvent for 30 minutes. This solvent is removed and replaced with an equal weight of 50% ethanol, and the ground material is extracted at reflux for a further 30 minutes. The operation is repeated once.

The 3 extracts obtained are combined (thus constituting a volume of about 19 litres), filtered through paper and then evaporated to dryness under reduced pressure.

A residue which weighs about 50 g if obtained, i.e. an approximate yield of 30% relative to the dry weight of the rhizomes. This extract contains the various shogaols present in the Alpinia galanga rhizomes ([3]-shogaol, [6]-shogaol and [8]-shogaol) and its content of [3]-shogaol is generally between 1 and 5% (w/w) depending on the rhizomes used.

EXAMPLE 2

PREPARATION OF A PURIFIED EXTRACT OF ALPINIA GALANGA RHIZOMES

50 g of a crude extract, prepared in accordance with Example 1, are taken up in 1 litre of distilled water and the mixture is boiled for 1 minute with constant stirring. Stirring is continued until complete homogenization of this extract is obtained, and the mixture is allowed to cool. It is then subjected to 4 successive counter-current extractions, each performed with 100 ml of ethyl ether.

The ether solutions are combined; anhydrous sodium sulphate is added to remove the water contained therein; they are filtered through paper and evaporated to dryness under reduced pressure.

A residue is thus obtained which weighs 6.8 g, i.e. a yield of about 4% relative to the dry weight of the rhizomes. This extract, which mainly contains [3]-shogaol, has a [3]-shogaol content which is generally greater than 75% (w/w).

EXAMPLE 3

PRODUCTION OF [3]-SHOGAOL

[3]-Shogaol can be obtained from Alpinia galanga rhizomes by preparing a crude extract of these rhizomes in accordance with Example 1, followed by purifying this extract in accordance with Example 2 and then subjecting the extract thus purified to successive elutions on columns of silica gel, for example in the following way.

100 g of a silica gel G60 and 500 ml of chloroform are added, with constant stirring, to 10 g of a purified extract, prepared in accordance with Example 2. Once this mixture is homogenous, it is evaporated to dryness under reached pressure so as to obtained a powder.

This powder is placed at the top of a column 10 cm in diameter and 50 cm in height, also containing silica gel G60 in petroleum ether. Elution is carried out first with petroleum ether until the residue is less than 0.1% (about 10 litres of petroleum ether are required to reach this stage), then with 12 litres of benzene and finally with 8 litres of chloroform.

The chloroform phase is evaporated to dryness under reduced pressure, to give about 2.3 g of residue. This residue is then subjected to preparation chromatography on a column 5 cm in diameter and 20 cm in height, filled with C18 silica gel, and using a water/acetonitrile mixture (70/30) as elution gradient. The fraction containing [3]-shogaol is eluted in a time of between 5 and 7 minutes at a flow rate of 30 ml/min.

The [3]-shogaol can be identified by high pressure liquid chromatography (HPLC) coupled to mass spectrometry.

FIG. 1 shows the mass spectrum of the [3]-shogaol obtained with a Waters Integrity.RTM. spectrometer with ionization by electron impact, coupled to HPLC carried out on a Nucleosil.RTM. column (4.6.times.150 mm, 3 .mu.m) with isocratic elution with an isopropanol/cyclohexane mixture (10/90).

EXAMPLE 4

PREPARATION OF A CRUDE EXTRACT OF ZINGIBER OFFICINALIS RHIZOMES

Using a procedure identical to the one described in Example 1, and starting with one kilogram of fresh Zingiber officinalis rhizomes, a residue is obtained weighing about 52 g, i.e. an approximate yield of 35% relative to the dry weight of the rhizomes.

This extract, which contains the gingerols present in the Zingiber officinalis rhizomes ([6]-gingerol, [8]-gingerol and [10]-gingerol), has a gingerol content which is generally between 1 and 5% (w/w) depending on the rhizomes used.

EXAMPLE 5

PREPARATION OF A PURIFIED EXTRACT OF ZINGIBER OFFICINALIS RHIZOMES

By subjecting 50 g of a crude extract prepared in accordance with Example 4 to purification under conditions identical to those described in Example 2, a residue is obtained which weighs 8.2 g, i.e. a yield of about 5.5% relative to the dry weight of the rhizomes. This extract has a gingerol content which is generally greater than 75% (w/w).

EXAMPLE 6

DEODORANT ACTIVITY OF A CRUDE EXTRACT OF ALPINIA GALANGA RHIZOMES

a) Systematic deodorant activity:

The systematic deodorant activity of a crude extract of Alpinia galanga rhizomes, prepared in accordance with Example 1, was tested on a group of 20 individuals by administering to them, via the oral route, this extract preformulated in the form of gel-capsules, and was compared with the activity of a placebo.

To do this, 1 kilogram of crude extract was intimately mixed with 1 kilogram of maltodextrin in a blade mill to ensure better homogeneity of the mixture and to obtain a mobile, non-sticky powder. This powder was then distributed in No. 0 gel-capsules so as to obtain a unit dosage of 250 mg of crude extract.

These gel-capsules were administered orally to a first group (group A) of 20 individuals comprising 10

men and 10 women between 17 and 62 years of age, for 10 days at a rate of 3 gel-capsules per day in a single intake, while a control group (group T), also composed of 10 men and 10 women and statistically comparable to the first, received, for 10 days and in a single oral intake, 3 gel-capsules per day each containing 250 mg of lactose.

The individuals of the two groups abstained from using local-application deodorants for the entire week preceding the start of the test, as well as throughout the duration of this test.

The efficacy of the crude extract in accordance with the invention and that of the placebo were evaluated by means of sensory analysis on the axillary zone of the individuals, in accordance with the tests conventionally used for deodorants, on the first day of the test (D0) before the first intake, on the 3rd and 6th days (D3 and D6), on the final day of the test (D10), as well as on the 3rd and 6th days following the end of this test (D13 and D16).

The results obtained expressed in the form of scores ranging from 0 to 5--the value 0 corresponding to an absence of deodorant efficacy and the value 5 to absolute deodorant efficacy (total absence of production of odours)--are given in Table 1 below.

TABLE 1

DAY	GROUP A	GROUP T
D0	0	0
D3	2	0
D6	4	0
D10	4	1
D13	3	0
D16	0	0

b) Local deodorant activity:

The local deodorant activity of a crude extract of Alpinia galanga rhizomes, prepared in accordance with Example 1, was also tested on a group of 20 individuals against placebo.

To do this, a first group (Group A) comprising 10 men and 10 women aged between 17 and 62 applied, by spraying onto the two axillary zones, for 3 days and at a rate of only one spray-application per day, 0.5 ml of a 50% ethanol solution comprising 1% of the said extract, while a second group (Group T) also composed of 10 men and 10 women and statistically comparable to the first, applied 0.5 ml of 50% ethanol under the same conditions.

All the individuals abstained from using local-application deodorants for the entire week preceding the start of the test, as well as throughout the duration of this test.

The efficacy of the crude extract in accordance with the invention and that of the placebo, were evaluated by means of sensory analysis of the axillary zone of the individuals, on the first day of the test before the first application (T0) and then 24 hours (T24), 48 hours (T48) and 72 hours (T72) after the start of this test.

The results, expressed in the form of scores ranging from 0 to 5--the value 0 corresponding to an absence of deodorant efficacy and the value 5 to absolute deodorant efficacy--are given in Table 2 below.

TABLE 2

HOURS	GROUP A	GROUP T

T0	0	0
T24	2	0
TD48	3	0
T72	3	0

EXAMPLE 7

DEODORANT ACTIVITY OF [3]-SHOGAOL

a) Systemic deodorant activity:

The systemic deodorant activity of [3]-shogaol was checked on a group of 20 individuals (Group A) against placebo (Group T) by means of a test similar to the one used according to Example 6 a) for evaluating the systemic efficacy of the crude extract of Alpinia galanga rhizomes, the only difference being that these individuals received gel-capsules containing 25 mg of [3]-shogaol instead of receiving gel-capsules containing 250 mg of the said extract.

The results obtained, also expressed in the form of scores ranging from 0 (absence of efficacy) to 5 (absolute efficacy), are given in Table 3 below.

TABLE 3

DAY	GROUP A	GROUP T
D0	0	0
D3	4	1
D6	5	0
D10	5	1
D13	4	0
D16	1	0

b) Local deodorant activity:

Preparation of a cosmetic solution of [3]-shogaol which can be used as a local deodorant:

10 g of [3]-shogaol are dissolved in 250 ml of 96% ethanol without heating. When dissolution is complete, 50 ml of monopropylene glycol and 200 ml of purified water are added. The solution obtained is filtered and then packaged in spray-containers.

Evaluation of the efficacy of the cosmetic solution of [3]-shogaol:

This was performed on a group of 20 individuals (Group A) versus placebo (Group T) by means of a test similar to the one used in Example 6 b) for assessing the deodorant activity which the crude extract of Alpinia galanga is capable of exhibiting locally.

However, in the present evaluation, the individuals of Group A applied, at each spray-application, 0.5 ml of cosmetic solution of [3]-shogaol while the individuals of Group T applied 0.5 ml of an ethanolic solution containing 10% monopropylene glycol and 40% water.

The results obtained during this evaluation, also expressed in the form of scores ranging from 0 (absence of efficacy) to 5 (absolute efficacy), are given in Table 4 below.

TABLE 4

HOURS	GROUP A	GROUP T
T0	0	0
T24	4	0
T48	4	1
T72	5	0

EXAMPLE 8

DEODORANT ACTIVITY OF A CRUDE EXTRACT OF ZINGIBER OFFICINALIS RHIZOMES

a) Systemic deodorant activity:

The systemic deodorant activity of a crude extract of Zingiber officinalis rhizomes, prepared in accordance with Example 4, was tested on a group of 20 individuals (Group A) versus placebo (Group T) by means of a test similar to the one used in Example 6 a) for evaluating the systemic efficacy of the crude extract of Alpinia galanga rhizomes.

The results obtained, also expressed in the form of scores ranging from 0 (absence of efficacy) to 5 (absolute efficacy) are given in Table 5 below.

TABLE 5

DAY	GROUP A	GROUP T
D0	0	0
D3	2	0
D6	2	0
D10	3	1
D13	2	0
D16	0	0

b) Local deodorant activity:

The local deodorant activity of a crude extract of Zingiber officinalis, prepared in accordance with Example 4, was also tested on a group of 20 individuals (Group A) versus placebo (Group T) by means of a test similar to the one used in Example 6 b) for evaluating the deodorant efficacy which the crude extract of Alpinia galanga is capable of exhibiting locally.

The results, also expressed in the form of scores ranging from 0 (absence of efficacy) to 5 (absolute efficacy), are given in Table 6 below.

TABLE 6

HOURS	GROUP A	GROUP T
T0	0	0
T24	2	0
T48	2	0
T72	2	0

EXAMPLE 9

DEODORANT ACTIVITY OF A PURIFIED EXTRACT OF ZINGIBER OFFICINALIS RHIZOMES

b) Systemic deodorant activity:

The systemic deodorant activity of a purified extract of Zingiber officinalis rhizomes, prepared in according with Example 5, was checked on a group of 20 individuals (Group A) versus placebo (Group T) by means of a test similar to the one used according to Example 6 a) for evaluating the systemic efficacy of the crude extract of Alpinia galanga rhizomes, the only difference being that these individuals received gel-capsules containing 25 mg of purified extract of Zingiber officinalis rhizomes instead of receiving gel-capsules containing 250 mg of crude extract of Alpinia galanga rhizomes.

The results obtained, also expressed in the form of scores ranging from 0 (absence of efficacy) to 5 (absolute efficacy), are given in Table 7 below.

TABLE 7

DAY	GROUP A	GROUP T
D0	0	0
D3	3	1
D6	3	0
D10	4	1
D13	2	0
D16	1	0

b) Local deodorant activity:

Preparation of a cosmetic solution from a purified extract of Zingiber officinalis which can be used as a local deodorant:

10 g of a purified extract, prepared in accordance with Example 5, are dissolved in 250 ml of 96% ethanol without heating. When dissolution is complete, 50 ml of monopropylene glycol and 200 ml of purified water are added. The solution obtained is filtered and then packaged in spray-containers.

Evaluation of the efficacy of the said cosmetics solution:

This was performed on a group of 20 individuals (Group A) versus placebo (Group T) by means of a test similar to the one used according to Example 6 b) for assessing the deodorant activity which the crude extract of Alpinia galanga rhizomes is capable of exhibiting locally.

However, in the present evaluation, the individuals of Group A applied, at each spray-application, 0.5 ml of cosmetic solution, while the individuals of Group T applied 0.5 ml of an ethanolic solution containing 10% monopropylene glycol and 40% water.

The results obtained during this evaluation, also expressed in the form of scores ranging from 0 (absence of efficacy) to 5 (absolute efficacy) are collated in Table 8 below.

TABLE 8

HOURS	GROUP A	GROUP T
T0	0	0
T24	3	0
T48	2	1
T72	3	0

As emerges from the account hereinabove, the invention is not limited in any way to the methods for forming it, implementing it and applying it which have just been described in greater detail: on the contrary, it embraces all the variants thereof which may occur to a person skilled in the art, without departing from the context or scope of the present invention.

Thus, the use of any shogaol or gingerol which would be obtained synthetically for the prepartion of a deodorant composition, and any deodorant composition containing such a shogaol or gingerol, also falls within the context of the invention.

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US006264928B1

(12) **United States Patent**
Jean et al.

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(45) **Date of Patent: Jul. 24, 2001**

(54) **USE OF SHOGAOLS AND GINGEROLS FOR PREPARING DEODORANT COMPOSITIONS**

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(52) **U.S. Cl.** **424/65**; 424/401

(58) **Field of Search** 424/65, 76.1, 401

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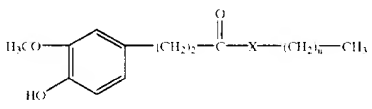
(57) **ABSTRACT**

A method is provided for suppressing body odors in a human by administering orally to the human or applying to the skin of the human, at least one compound chosen from the group consisting of shogaols and gingerols. The compound corresponds to the general formula:

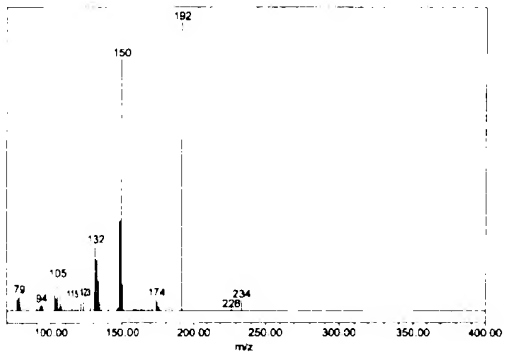


in which X represents:

either —CH=CH—, in which case n is equal to 1, 2, 4, 6, or 8;

—CH_2—CH(OH)—, in which case n is equal to 2, 4, 6 or 8.

22 Claims, 1 Drawing Sheet



US006274177B1

(12) **United States Patent**
Wu et al.

(10) **Patent No.: US 6,274,177 B1**
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(54) **METHOD OF PREPARING AN EXTRACT POTENT IN ANTI-INFLAMMATION AND ANTI-PLATELET AGGREGATION FROM *ZINGIBER OFFICINALE* AND PHARMACEUTICAL COMPOSITIONS CONTAINING SAID EXTRACT**

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(52) **U.S. Cl.** **424/756**; 424/773
(58) **Field of Search** 424/195.1, 773, 424/756

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BRS Computer Abstract JPAB JP07205777 Sugimoto et al "Synthesis Promoter for Neurotrophy Factor", Jan. 1995.*
BRS Computer Abstract JPAB JP406107556 Iwasaki et al "Chinese Analgesic Composed Exclusively of Herb Drug", Oct. 1995.*

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(57) **ABSTRACT**

A method of preparing an extract from *Zingiber officinale*, which is potent in anti-inflammation and anti-platelet aggregation, includes the following steps: a) preparing a crude liquid from rhizomes of ginger by extraction with an organic solvent or by distillation with steam; b) introducing the crude liquid to a reverse phase chromatography column, and eluting the column with water, a first eluent and a second eluent having a polarity weaker than that of the first eluent but stronger than that of chloroform, so that a first eluate resulting from elution of the first eluent and a second eluate resulting from elution of the second eluent are obtained; c) removing the first eluent from the first eluate by evaporation, so that a first concentrated eluate is obtained and is able to used as the potent extract; and d) removing the second eluent from the second eluate by evaporation, so that a second concentrated eluate is obtained and is able to used as the potent extract.

37 Claims, No Drawings

METHOD OF PREPARING AN EXTRACT POTENT IN ANTI-INFLAMMATION AND ANTI-PLATELET AGGREGATION FROM *ZINGIBER OFFICINALE* AND PHARMACEUTICAL COMPOSITIONS CONTAINING SAID EXTRACT

FIELD OF THE INVENTION

The present invention is related to a method of preparing an extract potent in anti-inflammation and anti-platelet aggregation from *Zingiber officinale*.

BACKGROUND OF THE INVENTION

Chinese crude drugs or spices eg. *Zingiber officinale, Eugenia caryophyllata, Allium sativum*, have been used in medicine and in flavoring foods. Crude ginger is used as an anti-emetic and expectorant, an anti-tussive and accelerator of the digestive organs. Semi-dried old crude ginger is also used for stomachache, chest pain, low back pain, cough, common cold and as a cure for a form of edema being called "stagnate of water". Zingerone is the major component which accounts for the spicy character of ginger; gingerol and shogaol are other pungent components in ginger. Gingerol has cardio-tonic action, suppresses the contraction of isolated portal veins in mice, and modulates the eicosanoid-induced contraction of mouse and rat blood vessels. Shogaol exhibits pressor response. Both gingerol and shogaol are mutagenic, whereas zinger and zingerone have been found to exhibit antimutagenic activity. Shogaol has inhibitory activity on the carrageenin-induced paw edema and platelet aggregation [U.S. Pat. No. 5,804,603, Background of the Invention].

Heretofore, many reports have shown that *Zingiber officinale* exhibits various physiological activities. Typical examples include a cancer metastasis suppressing agent disclosed in Japan patent publication No. 7-258104; a synthesis promoter for neurotropic factor, which is effective for nerve deteriorative diseases such as Alzheimer's dementia or Parkinson's disease, disclosed in Japan patent publication No. 7-25777; an anti-rheumatic agent disclosed in Japan patent publication No. 6-293653, U.S. Pat. Nos. 5,494,668 and 5,683,698; an antimicrobial composition disclosed in Japan patent publication No. 6-227931; and an analgesic composition disclosed in Japan patent publication No. 6-107556. Ginger contains 1–4% essential oil (oleoresin). During the last 45 years many chemical investigations have been carried out on the constituents of the essential oil. Altogether more than 200 different volatiles have been identified in essential oil wherein the pharmacological activity is confined. The essential oil contains a mixture of various terpenes as well as some other non-terpenoid compounds. Although this is mostly speculative, the experimental data and observations suggest that ginger inhibits both the cyclooxygenase and lypoxygenase products, i.e. it can be a dual inhibitor of eicosanoid synthesis. In all 56 patients (28 with rheumatoid arthritis, 18 with osteoarthritis and 10 with muscular discomfort) used powdered ginger against their afflictions. Amongst the arthritis patients more than three-quarters experienced, to varying degrees, relief in pain and swelling. All the patients with muscular discomfort experienced relief in pain. None of the patients reported adverse effects during the period of ginger consumption which ranged from 3 months to 2 5 years. (Srivastava and Mustafa, Medical Hypotheses; 1992; 39 342–348).

Non-steroidal anti-inflammatory drugs have three major actions, all of which are related to inhibition of cyclo-

oxygenase resulting in decreased formation of prostanoids. Firstly, an anti-inflammatory action achieved by reduced production of vasodilator prostaglandins (PGE2, PGI2) which means less vasodilation and, indirectly less edema. Secondly, an analgesic effect achieved by reduced prostaglandin production (less sensitization of nociceptic nerve endings to the inflammatory mediators bradykinin and 5-hydroxytryptamine). Thirdly, an antipyretic effect which is probably due to a decrease in the mediator PGE2 generated in response to inflammatory pyrogens, much as interleukin-1. Since ginger inhibits prostanoid synthesis and also products of 5-lipoxygenase, its ameliorative effects in arthritis and muscular discomforts could be related to reduced formation of prostanoids and leukotrienes. Because of such a possibility a decrease in the carageenan-induced edema formation in the rat's paw after 3 g of ginger extract administration has been demonstrated and the potency of the extract in the acute inflammation test appears to be comparable to that exhibited by acetyl salicylic acid reported in the same study. (Mascolo N. et al Journal of Ethnopharmocology 1989, 27, 129–140).

SUMMARY OF THE INVENTION

The present invention provides extracts from rhizomes of ginger which show an activity in an in vitro anti-platelet aggregation test and an inhibitory activity on the carrageenin-induced paw edema. The extracts are prepared by extracting rhizomes of ginger with an organic solvent (such as ethyl ether, acetone, methanol and ethanol) or supercritical CO_2, or by steam distilling rhizomes of ginger to obtain a crude liquid, and subjecting said crude liquid to a reverse phase chromatography to obtain the extracts containing shogaols, gingerols and/or dehydrogingerdione.

DETAILED DESCRIPTION OF THE INVENTION

As introduced in the Background of the Invention, ginger has been used for anti-inflammation and pain relief.

The present invention is to provide an effective method of preparing a product potent in anti-inflammation and in anti-platelet aggregation from rhizomes of ginger. The potent product prepared in accordance with the method of the present invention has a substantially constant composition, so that the pharmaceutical effects thereof are definite.

The effective method of preparing product potent in anti-inflammation and in anti-platelet aggregation from rhizomes of ginger according to the present invention comprises the following steps:

a) preparing a crude liquid from rhizomes of ginger;

b) introducing the crude liquid to a reverse phase chromatography column, and eluting the column with water, a first eluent and a second eluent in sequence, said second eluent having a polarity weaker than that of the first eluent but stronger than that of chloroform, so that a first eluate resulting from elution of the first eluent and a second eluate resulting from elution of the second eluent are obtained;

c) removing the first eluent from the first eluate by evaporation, so that a first concentrated eluate is obtained and is able to be used as the potent product; and

d) removing the second eluent from the second eluate by evaporation, so that a second concentrated eluate is obtained and is able to be used as the potent product;

wherein step a) comprises steps i) to iv), or comprises step I), step I'), or step I"), wherein said steps i) to iv) are:

i) shedding fresh rhizomes of ginger and filtering the resulting mixture to obtain a filtrate and a residue;

ii) extracting the filtrate with a first organic solvent, recovering the resulting extraction solution of the first organic solvent, and evaporating the first organic solvent from the extraction solution to obtain a first concentrated extraction solution;

iii) extracting the residue with a second organic solvent, recovering the resulting extraction solution of the second organic solvent, and evaporating the second organic solvent from the extraction solution to obtain a second concentrated extraction solution; and

iv) combining the first concentrated extraction solution and the second concentrated extraction solution to obtain the crude liquid;

said step I) is:

I) extracting powder of dried rhizomes of ginger with the second organic solvent, recovering the resulting extraction solution of the second organic solvent, and evaporating the second organic solvent from the extraction solution to obtain the crude liquid;

said step I') is:

I') steam distilling powder of dried rhizomes of ginger, and concentrating the resulting distillate by evaporation to obtain the crude liquid; and

said step I") is:

I") extracting powder of dried rhizomes of ginger with supercritical CO_2, recovering the resulting extraction solution of the supercritical CO_2, and evaporating CO_2 from the extraction solution to obtain the crude liquid.

The product potent in anti-inflammation and in anti-platelet aggregation prepared according to the method of the present invention preferably comprises 0–10 mg 6-shogaol per gram of the product, 1–150 mg 6-gingerol per gram of the product, and 0–40 mg 6-dehydrogingerdione per gram of the product.

The present invention also provides an anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of said crude liquid prepared in step a) of the method of the present invention, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

The present invention also provides a pharmaceutical composition for the inhibition of aggregation of platelets, which comprises a therapeutically effective amount of said crude liquid prepared in step a) of the method of the present invention, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

The present invention also provides an anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of said product prepared according to the method of the present invention, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient. Preferably, said product prepared according to the method of the present invention is the first concentrated eluate prepared in step c). Alternatively, said product prepared according to the method of the present invention is the second concentrated eluate prepared in step d).

The present invention also provides a pharmaceutical composition for the inhibition of aggregation of platelets, which comprises a therapeutically effective amount of said product prepared according to the method of the present invention, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient. Preferably, said product prepared according to the method of the present invention is the first concentrated eluate prepared in step c). Alternatively, said product prepared according to the method of the present invention is the second concentrated eluate prepared in step d).

Preferably, said first eluent is methanol, and said second eluent is acetone.

Preferably, step a) of the method of the present invention comprises steps i) to iv).

Preferably, said first organic solvent is ethyl ether.

Preferably, said second organic solvent is acetone, methanol, ethanol or a combination thereof. More preferably, said second organic solvent is acetone.

Preferably, step a) of the method of the present invention comprises step I).

Preferably, step a) of the method of the present invention comprises step I').

Preferably, step a) of the method of the present invention comprises step I").

A suitable reverse phase chromatography column for use in the method of the present invention includes (but is not limited thereto) a reverse phase chromatography column packed with a porous resin, for examples Diaion HP-20 (Mitsubishi Co.), Sephadex LH-20 (Pharmicia Co.) and RP-18 (Nacalai tesque Co.).

Without further elaboration, it is believed that the above description has adequately enabled the present invention. The following specific examples are, therefore, to be construed as merely illustrative, and not limitations on the remainder of the disclosure in any way whatsoever.

DETERMINATION OF ACTIVE INGREDIENTS

In the following examples, high performance liquid chromatography (abbreviated as HPLC) was used to determine the active ingredients of the products prepared therein. HPLC spectra were recorded on a HPLC instrument (HPLC Shimadzu LC-10AT, Japan) using a Cosmosil 5C-18 column (250 mm×4.6 mm, packed with particles having 5 μm diameter) by an elution method. An HPLC sample was prepared by diluting an appropriate amount of a product with a mobile phase solution (hydrogen cyanide:water= 65:35, V/V) to 25 ml, and filtered with a 0.25 μm membrane. The filtrate was introduced into the HPLC column, and eluted with the mobile phase solution. An UV detector (Shimadzu SPD-6AV, Japan) was used to detect the absorption of the eluate at 230 nm.

EXAMPLE 1

2100 g of fresh rhizomes of ginger were shredded and filtered to obtain a filtrate and a residue. 500 ml of the filtrate was extracted with 500 ml ethyl ether three times, the organic phase layers were separated from the aqueous phase layers, and combined. Ethyl ether was evaporated from the combined extraction solution in vacuo to obtain a concentrated ethyl ether extraction product (I-OE). The ginger residue was extract with 3000 ml acetone three times, the extraction solutions were recovered by filtration, and combined. Acetone was evaporated from the combined extraction solution in vacuo to obtain a concentrated acetone extraction product (I-O) (14.5 g). To a reverse phase chromatography column 300 mm×30 mm packed with 180 g Diaion HP-20 resin having a diameter of 500 μ–800 μ 7 g of a mixture of the concentrate ethyl ether extraction product (I-OE) and the concentrated acetone extraction product (I-O)

was injected. 1500 ml water, 2500 ml methanol, 2000 ml acetone and 2000 ml chloroform were used to carry out elution. The water eluate, methanol eluate, acetone eluate and chloroform eluate were collected separately, and concentrated in vacuo to obtain 0.27 g concentrated water eluate (I-OW), 1.45 g concentrated methanol eluate (I-OM), 2.68 g concentrated acetone eluate (I-OA), and 0.83 g concentrated chloroform eluate (I-OC). The amounts (mg) of 6-shogaol, 6-gingerol and 6-dehydrogingerdione per gram of the I-O, I-OM and I-OA determined by HPLC are listed in Table 1.

TABLE 1

Content (mg/g)	I-O	I-OM	I-OA
6-shogaol	1.10 ± 0.14	1.15 ± 0.0	—
6-gingerol	59.98 ± 0.99	103.37 ± 8.57	2.51 ± 0.89
6-dehydrogingerdione	7.68 ± 0.42	8.94 ± 0.41	—

EXAMPLE 2

500 g of shade dried rhizomes of ginger were pulverized and the resulting powder was extracted with 30 L acetone trice (each time with 10 L). The three extraction solutions were combined together after filtration, and then concentrated in vacuo to obtain 24 g of concentrated acetone extraction product (II-O). To a reverse phase chromatography column packed with 600 g Diaion HP-20 resin 20 g of the concentrated acetone extraction product (II-O) was injected, which was then eluted with 4 L water, 6.5 L methanol, 15 L acetone and 5 L chloroform in sequence. The water eluate, methanol eluate, acetone eluate and chloroform eluate were collected separately, and concentrated in vacuo to obtain 2.5 g concentrated water eluate (II-OW), 7.1 g concentrated methanol eluate (II-OM), 6.9 g concentrated acetone eluate (II-OA), and 3.5 g concentrated chloroform eluate (II-OC). The amounts (mg) of 6-shogaol, 6-gingerol and 6-dehydrogingerdione per gram of the II-O, II-OM and II-OA determined by HPLC are listed in Table 2.

TABLE 2

Content (mg/g)	II-O	II-OM	II-OA
6-shogaol	1.98 ± 0.00	4.96 ± 0.00	—
6-gingerol	43.06 ± 0.84	70.87 ± 1.85	2.54 ± 0.00
6-dehydrogingerdione	9.33 ± 0.85	19.15 ± 4.57	2.35 ± 0.28

EXAMPLE 3

10 Kg of shade dried rhizomes of ginger were pulverized and the resulting powder was steam distilled for five hours. The distillate was concentrated in vacuo to obtain 410 g of concentrated distillate (III-O). To a reverse phase chromatography column packed with 600 g Diaion HP-20 resin 20 g of the concentrated distillate (III-O) was injected, which was then eluted with 4.5 L water, 4.5 L methanol, 3 L acetone and 5 L chloroform in sequence. The water eluate, methanol eluate, acetone eluate and chloroform eluate were collected separately, and concentrated in vacuo to obtain 0.03 g concentrated water eluate (III-OW), 14.5 g concentrated methanol eluate (III-OM), 0.85 g concentrated acetone eluate (III-OA), and 0.2 g concentrated chloroform eluate (III-OC). The concentrated distillate (III-O) contains no 6-shogaol, 6-gingerol and 6-dehydrogingerdione determined by HPLC.

EXAMPLE 4

10 g of powder of shade dried rhizomes of ginger was extracted with 1000 ml acetone at 50° C. for two hours. The extraction solution was separated and concentrated in vacuo (40° C., 75 mmHg) to obtain a concentrated acetone extraction product (IV-O). The color and viscosity of the product (IV-O) together with its yield are listed in Table 3.

EXAMPLE 5

10 g of powder of shade dried rhizomes of ginger was steam distilled, and the oily distillate after being separated from the aqueous distillate was freeze dried to obtain an oily extract (V-O). The color and viscosity of the oily extract (V-O) together with its yield are listed in Table 3.

EXAMPLE 6

To 10 g of powder of shade dried rhizomes of ginger in a 250 ml extraction chamber CO_2 was introduced at a flow rate of 45 L/min, wherein the chamber pressure was controlled at 2500 to 4000 psia with a high pressure pump (Model No. EK-1, LEWA Co., US) and the chamber temperature was maintained at 35–60° C. with a heat exchanger (Model No. H-2410, HOTEC Co., US) and an exterior circulation system. The extraction was stopped when the volume of CO_2 introduced reached 300 L, and a supercritical CO_2 extraction product (VI-O) was obtained after evaporation of CO_2. The color and viscosity of the product (VI-O) together with its yield are listed in Table 3. The contents of pungent components determined by HPLC are listed in Table 4.

TABLE 3

	IV-O	V-O	VI-O
L*	87.6	80.4	96.3
A*	−9.1	−0.1	−9.6
B*	31.1	9.6	22.0
Viscosity (cPs)	15.6	11.8	12.1
Yield (%)	3.8	2.2	3.9

*the values of L, A, and B were determined by using a Σ90 color measuring system, (Nippon Denshoku Inc, Co., Ltd., Japan), wherein L represents lightness, A is the red/green difference and B is the yellow/blue difference.

TABLE 4

Content (mg/g)	VI-O
6-shogaol	17.30 ± 0.00
6-gingerol	26.29 ± 0.00
6-dehydrogingerdione	19.20 ± 1.19

EXAMPLE 7

Antiplatelet Assay

Blood, collected from the marginal ear vein of rabbits was mixed with EDTA (100 mM) in a volume ratio of 14:1 and centrifuged at 90 g for 10 min at room temperature to obtain platelet-rich plasma. The latter was further centrifuged at 500 g for 10 min, the upper plasma-rich layer was removed therefrom, and the remaining bottom layer was suspended with Tyrode's solution containing 2 mM EDTA but no calcium. The suspension was further centrifuged at 500 g for 10 min and the platelets were suspended with Tyrode's solution without EDTA. After centrifugation at the same conditions, the platelets were suspended with Tyrode's solution having the following compositions (mM): NaCl (136.8), KCl (2.8), $NaNCO_3$ (11.9), $MgCl_2$ (1.1), NaH_2PO_4

(0.33), $CaCl_2$ (1.0), glucose (1 1.2) and borine serum albumin (0.35%). Platelet numbers were determined with a Coulter Counter (Model ZM) and adjusted to 4.5×10^8 platelets/ml.

TABLE 5

The inhibitory effects of ginger extracts on platelet aggregation induced by arachidonic acid and collagen[a)]

Ginger extracts	Concentration for 50% inhibitory effect (μg/ml) Arachidonic acid	Collagen
I-O	3.8 ± 0.8	5.5 ± 0.4
I-OM	1.7 ± 0.3	2.7 ± 0.4
II-O	3.1 ± 0.5	6.5 ± 1.2
II-OA	10.9 ± 3.2	21.8 ± 2.2
II-OC	6.9 ± 0.7	16.6 ± 4.3
II-OM	2.0 ± 0.2	6.9 ± 2.4

[a)]Platelets were incubated with ginger extracts or 0.5% DMSO (Control) at 37° C. for 3 min, then arachidonic acid (100 μM) or collagen (10 μg/ml) was added to trigger aggregation. Aspirin and Indomethacin are positive controls. The percentage of inhibitory effect is calculated as follows: {[(degree of inhibition of Control) - (degree of inhibition of ginger extract)]/(degree of inhibition of Control)} × 100%
Values are presented as mean ± S.E., n = 3–6.

EXAMPLE 8

Evaluation of Inhibitory Activity on the Carrageenin-induced Paw Edema

Inhibitory activity on the carrageenin-induced paw edema was conducted according to the method reported by Winter, C. A. et al. (Winter C. A. et al., Proc. Soc. Exper. Biol. Med. 111: 544–547, 1962.). Male Wistar mice weighing 150±20 g without feeding for one night were injected at left rear paws thereof with 0.1 ml of 1% carrageenin suspension followed by rubbing test samples or vehicle as control on the left rear paws evenly (10 mg/paw). Three hours later, the volumes of the rear paws were determined by using a volume scanner (Cat. #7150, UGO Basil, Italy), and the difference between the left rear paw and the right rear paw was used an index of the carrageenin-induced paw edema.

TABLE 6

Inhibitory activity on the carrageenin-induced paw edema of ginger extracts

Treatment	Dosage (mg/paw)	Inhibitory activity on the carrageenin-induced paw edema (%)
I-O	10	18
I-OE	10	19
I-OM	10	29
I-OA	10	25
II-O	10	18
II-OW	10	0
II-OM	10	26
II-OA	10	25
II-OC	10	8
III-O	10	0
III-OM	10	11
III-OA	10	15
[6]-dehydrogingedione	5	26

1. Inhibitory activity on the carrageenin-induced paw edema (%) was calculated as follows: {(average degree of edema of mice in the control group) - (average degree of edema of mice in the test group)/(average degree of edema of mice in the control group)} × 100%
2. Values are presented as mean ± S.E., n = 3–6.

What is claimed is:

1. A method of preparing a product potent in anti-inflammation or in anti-platelet aggregation from rhizomes of *Zingiber officinale* comprising the following steps:

a) preparing a crude liquid from rhizomes of *Zingiber officinale;*

b) introducing the crude liquid to a reverse phase chromatography column, and eluting the column with water, a first eluent and a second eluent in sequence, said second eluent having a polarity weaker than that of the first eluent but stronger than that of chloroform, so that a first eluate resulting from elution of the first eluent and a second eluate resulting from elution of the second eluent are obtained;

c) removing the first eluent from the first eluate by evaporation, so that a first concentrated eluate is obtained and is able to be used as the potent product; and

d) removing the second eluent from the second eluate by evaporation, so that a second concentrated eluate is obtained and is able to used as the potent product;

wherein step a) comprises steps i) to iv), or comprises step I), step I'), or step I"), wherein said steps i) to iv) are:

i) shedding fresh rhizomes of *Zingiber officinale* and filleting the resulting mixture to obtain a filtrate and a residue;

ii) extracting the filtrate with a first organic solvent, recovering the resulting extraction solution of the first organic solvent, and evaporating the first organic solvent from the extraction solution to obtain a first concentrated extraction solution;

iii) extracting the residue with a second organic solvent, recovering the resulting extraction solution of the second organic solvent, and evaporating the second organic solvent from the extraction solution to obtain a second concentrated extraction solution; and

iv) combining the first concentrated extraction solution and the second concentrated extraction solution to obtain the crude liquid;

said step I) is:

I) extracting powder of dried rhizomes of *Zingiber officinale* with the second organic solvent, recovering the resulting extraction solution of the second organic solvent, and evaporating the second organic solvent from the extraction solution to obtain the crude liquid;

said step I') is:

I') steam distilling powder of dried rhizomes of *Zingiber officinale*, and concentrating the resulting distillate by evaporation to obtain the crude liquid; and

said step I") is:

I") extracting powder of dried rhizomes of *Zingiber officinale* with supercritical CO_2, recovering the resulting extraction solution of the supercritical CO_2, and evaporating CO_2 from the extraction solution to obtain the crude liquid.

2. The method according to claim 1, wherein the product potent in anti-inflammation or in anti-platelet aggregation comprises 0–10 mg 6-shogaol per gram of the product, 1–150 mg 6-gingerol per gram of the product, and 0–40 mg 6-dehydrogingerdione per gram of the product.

3. The method according to claim 1, wherein said first eluent is methanol, and said second eluent is acetone.

4. The method according to claim 3, wherein step a) comprises steps i) to iv).

5. The method according to claim 4, wherein said first organic solvent is ethyl ether.

6. The method according to claim 4, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

7. The method according to claim 6, wherein said second organic solvent is acetone.

8. The method according to claim 3, wherein step a) comprises step I).

9. The method according to claim 8, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

10. The method according to claim 9, wherein said second organic solvent is acetone.

11. The method according to claim 3, wherein step a) comprises step I').

12. The method according to claim 3, wherein step a) comprises step I").

13. The method according to claim 3, wherein said reverse phase chromatography column is packed with a porous resin.

14. An anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of a crude liquid prepared in step a) of the method according to claim 1, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

15. The pharmaceutical composition according to claim 14, wherein step a) comprises steps i) to iv).

16. The pharmaceutical composition according to claim 15, wherein said first organic solvent is ethyl ether.

17. The pharmaceutical composition according to claim 16, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

18. The pharmaceutical composition according to claim 17, wherein said second organic solvent is acetone.

19. The pharmaceutical composition according to claim 14, wherein step a) comprises step I).

20. The pharmaceutical composition according to claim 19, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

21. The pharmaceutical composition according to claim 20, wherein said second organic solvent is acetone.

22. The pharmaceutical composition according to claim 14, wherein step a) comprises step I').

23. The pharmaceutical composition according to claim 14, wherein step a) comprises step I").

24. A pharmaceutical composition for the inhibition of aggregation of platelet, which comprises a therapeutically effective amount of the first concentrated eluate prepared in step c) of the method according to any one of claims 1 to 13, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

25. An anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of the first concentrated eluate prepared in step c) of the method according to any one of claims 1 to 13, as an active ingredient in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

26. An anti-inflammation pharmaceutical composition comprising a therapeutically effective amount of the second concentrated eluate prepared in step d) of the method according to any one of claims 1 to 13, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

27. A pharmaceutical composition for the inhibition of aggregation of platelet, which comprises a therapeutically effective amount of said crude liquid prepared in step a) of the method according to claim 1, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

28. The pharmaceutical composition according to claim 27, wherein step a) comprises steps i) to iv).

29. The pharmaceutical composition according to claim 28, wherein said first organic solvent is ethyl ether.

30. The pharmaceutical composition according to claim 28, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

31. The pharmaceutical composition according to claim 30, wherein said second organic solvent is acetone.

32. The pharmaceutical composition according to claim 27, wherein step a) comprises step I).

33. The pharmaceutical composition according to claim 32, wherein said second organic solvent is acetone, methanol, ethanol or a combination of them.

34. The pharmaceutical composition according to claim 33, wherein said second organic solvent is acetone.

35. The pharmaceutical composition according to claim 27, wherein step a) comprises step I').

36. The pharmaceutical composition according to claim 27, wherein step a) comprises step I").

37. A pharmaceutical composition for the inhibition of aggregation of platelet, which comprises a therapeutically effective amount of the second concentrated eluate prepared in step d) of the method according to any one of claims 1 to 13, as an active ingredient, in admixture with a pharmaceutically acceptable carrier or diluent for the active ingredient.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,274,177 B1
DATED : August 14, 2001
INVENTOR(S) : Tian-Shung Wu, Sheng-Chu Kuo, Che-Ming Teng and Feng-Nien Ko

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page,
Item [73], the name of the Assignee should read: -- **Pharmaceutical Industry Technology and Development Center Taipei Hsien (TW)**

Signed and Sealed this

Twenty-fifth Day of June, 2002

Attest:

Attesting Officer

JAMES E. ROGAN
Director of the United States Patent and Trademark Office